Table I. Measures of Molecular Mobility and Acid-Catalyzed Proton Exchange in the System t-BuOH–H_2O at 25°

Property	Mole % t-BuOH 0.00	Mole % t-BuOH 11.47	Ratio
η, Cp	0.89	3.43	3.86
$1/T_1$ for OH protons, sec^{-1}	0.39^a	0.90^a	2.3
E_{act}, kcal, for T_1	3.6	6.6	...
$1/T^1$ for ^{17}O in $H_2{}^{17}O$, sec^{-1}	$160^{a,b}$	440^a	2.75
$R_{WW}/[H^+][H_2O]$, sec^{-1} M^{-1}	7.1×10^{9c}	4.6×10^9	1.5_5

[a] All T_1 measurements were made in air-saturated solvent. [b] Reference 11, and B. B. Garrett, A. B. Denison, and S. W. Rabideau, *J. Phys. Chem.*, **71**, 2606 (1967). [c] The value listed in this table is $2k_1/3$, as reported by Meiboom.[2]

solvation of H_3O^+ in the t-BuOH–HOH system. There is no doubt that the specific rate for reaction between H_3O^+ and alcohol is only slightly smaller than that for the reaction between H_3O^+ and water. This is possible only if the distribution of molecules around the H_3O^+ ion is nearly statistical; that is, a model of strong preferential solvation of H_3O^+ by water molecules seems to be ruled out.

Regarding R_{WW}, our data permit comparison of the specific rate in pure water with that in 11.47 mole % t-BuOH–HOH. As shown in Table I, the specific rate decreases by a factor of 1.55, while the viscosity increases by a factor of 3.86. Thus the "Walden product," (specific rate)·η, increases by 2.5, in good qualitative agreement with the Walden product for the anomalous conductance. On the other hand, the solvent effect on the specific rate is in better agreement with that on the OH-proton T_1, or on the ^{17}O T^1, which in a rough way measure the rate of rotation of the water molecules.

Proton Exchange and Solvation of Imidazole in *t*-Butyl Alcohol-Water Mixtures[1]

Earle K. Ralph and Ernest Grunwald

Contribution from the Lecks Chemical Laboratories, Brandeis University, Waltham, Massachusetts 02154. *Received October 10, 1968*

Abstract: Effects of specific solvation on proton transfer of imidazolium ion (ImH^+) have been studied in t-BuOH–HOH mixtures by nmr measurements of proton-exchange rates and by potentiometric measurements of pK_A. Processes that make significant kinetic contributions to proton exchange are acid dissociation, the mechanism of which is found to be analogous to that in water, and the termolecular reactions, $ImH^+ + (OH)H + Im \rightarrow Im + HOH + HIm^+$ (k_{2W}), and $ImH^+ + (OBu\text{-}t)H + Im \rightarrow Im + HOBu\text{-}t + HIm^+$ (k_{2A}). In 11.47 mole % t-BuOH at 25°, $k_{2W} = 2.0 \times 10^8$ sec^{-1} M^{-1} and $k_{2A} = 1.57 \times 10^7$ sec^{-1} M^{-1}. The magnitude of k_{2W}/k_{2A} is very similar to that of the $[H_2O]/[t\text{-BuOH}]$ mole ratio, suggesting that the relative abundance of the respective termolecular encounter complexes is nearly statistical. k_{2W} is strikingly greater in the t-BuOH–HOH mixtures than in water.

Kinetic analysis of proton exchange accompanying fast proton-transfer reactions can provide new information about solvation, especially when the rate-determining step is the solvation or desolvation of one of the reacting species.[2] The present paper is the first of a series in which we use this technique to study preferential solvation in t-butyl alcohol–water mixtures. This system is suitable for such a study because precise nmr measurements of the rates of exchange are possible. Rates of exchange can be measured separately for alcohol OH protons and water OH protons. The system is chemically interesting, and thermodynamic studies suggest that specific solvation effects may be pronounced.[3] Our own interest would center on the kinetic effects of specific solvation, especially on the relative rates of breaking of solute–water and solute–HOBu-t hydrogen-bonded complexes. We would expect those rates to be quite different if the solute–solvent interaction is dominated by London dispersion forces.[4]

In this paper we report a study of proton exchange of imidazolium ion (ImH^+) in t-BuOH–water mixtures containing 9.98 and 11.47 mole % t-BuOH. Rates were measured by the nmr method at temperatures ranging

---

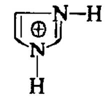
(1) Work supported in part by the National Science Foundation and by the Petroleum Research Fund of the American Chemical Society. Grateful acknowledgment is made to that foundation and to the donors of that fund.

(2) W. J. Alberty, *Progr. Reaction Kinetics*, **4**, 353 (1967).

(3) E. M. Arnett and D. R. McKelvey, *J. Amer. Chem. Soc.*, **88**, 5031 (1966).

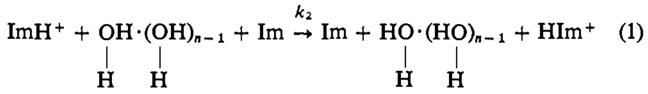
(4) E. Grunwald and E. K. Ralph, *ibid.*, **89**, 4405 (1967).

from 10 to 35° and hydrogen ion concentrations from 10^{-7} to 3.4 M HCl. We also report measurements of the acid dissociation constant, K_a, of imidazolium ion.



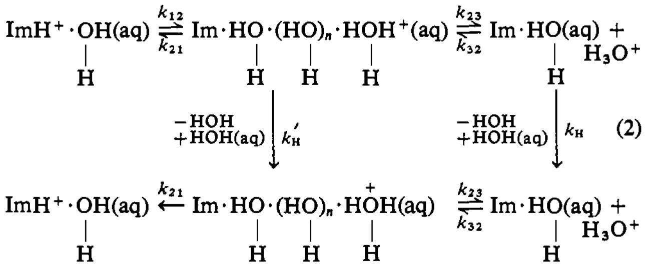
ImH^+

Proton exchange between ImH^+ and water in the absence of alcohol is reported in preceding communications.[5,6] That system shows two unusual features: (1) proton exchange between ImH^+, Im, and water (eq 1) is partly higher than termolecular, the average value of n



$$\underset{}{ImH^+} + \underset{\mathrm{H}}{\overset{}{O}}\mathrm{H}\cdot(\underset{\mathrm{H}}{O}\mathrm{H})_{n-1} + Im \xrightarrow{k_2} Im + H\underset{\mathrm{H}}{O}\cdot(H\underset{\mathrm{H}}{O})_{n-1} + HIm^+ \quad (1)$$

being 1.4;[6] (2) proton exchange between ImH^+ and water consists of two kinetically resolvable processes. One of these is acid dissociation *via* an ionized intermediate; the other is a cyclic process that is thought to involve the same intermediate,[5] as shown in eq 2.



$$\begin{array}{ccccc}
ImH^+\cdot\underset{\mathrm{H}}{O}H(aq) & \underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}} & Im\cdot H\underset{\mathrm{H}}{O}\cdot(H\underset{\mathrm{H}}{O})_n\cdot H\underset{\mathrm{H}}{O}H^+(aq) & \underset{k_{32}}{\overset{k_{23}}{\rightleftharpoons}} & Im\cdot H\underset{\mathrm{H}}{O}(aq) + H_3O^+ \\
 & & \Big\downarrow {\scriptstyle -HOH,\ +HOH(aq)}\ k_H' & & \Big\downarrow {\scriptstyle -HOH,\ +HOH(aq)}\ k_H \\
ImH^+\cdot\underset{\mathrm{H}}{O}H(aq) & \overset{k_{21}}{\longleftarrow} & Im\cdot H\underset{\mathrm{H}}{O}\cdot(H\underset{\mathrm{H}}{O})_n\cdot H\overset{+}{\underset{\mathrm{H}}{O}}H(aq) & \underset{k_{32}}{\overset{k_{23}}{\rightleftharpoons}} & Im\cdot H\underset{\mathrm{H}}{O}(aq) + H_3O^+
\end{array} \quad (2)$$

We find that proton exchange in the t-BuOH mixtures is described by the same rate law as in water, but there are differences in solvent participation: reaction 1 now consists of two resolvable components, with rate constants k_{2W} and k_{2A}, in which the participating solvent molecule is either water or t-BuOH. In 11.47 mole % t-BuOH the reaction with water is termolecular, and k_{2W} is greater than k_2 in pure water, in spite of the increased solvent viscosity and smaller water concentration. k_{2A}/k_{2W} is about one-half the alcohol:water mole ratio.

Proton exchange between ImH^+ and OH protons of the mixed solvent consists of two kinetically resolvable processes, as in water. The new data further support the mechanism shown in eq 2.

Results

pK_a Measurements. Acid dissociation constants were measured by the differential potentiometric method[7] with an accuracy of about 1%. Results are listed in Table I. From the temperature variation we find that in 11.47 mole % t-BuOH, $\Delta H° = 6.5 \pm 0.5$ kcal. In water, $\Delta H°$ is 8.0 ± 0.2 kcal.[5]

NH-OH Exchange. The rate measurements reported in this section were done at pH < 4. In the absence of imidazole the alcohol OH-water OH resonance is a sharp single line, because the H^+-catalyzed exchange is very fast. The broadening of this resonance that is observed when imidazolium ion is present must, therefore, be ascribed to NH-OH exchange. The rate, R_{NH}, was calculated by precisely the same method as in water.[5]

Table I. Acid Dissociation of Imidazole in t-BuOH-Water Mixtures

t-BuOH, mole %	Temp, °C	pK_a°[b]
11.47	11.0	6.741
11.47	18.0	6.637
11.47	25.0	6.508
9.98	25.0	6.530
0	25.0	6.976[a]

[a] Reference 5. [b] pK_a extrapolated to infinite dilution on the basis of the equation pK_a = pK_a° + B[ImHCl]. B was always between 0 and 0.1. The term B[ImHCl] was always negligible in the kinetic experiments, where [ImHCl] < 0.08 M.

Unfortunately rates were not measurable with uniform accuracy throughout the experimental range. When $R_{NH}/2[ImH^+] = \delta$ (the NH-OH chemical shift in radians), the exchange broadening, Δ, is at a maximum and $d\Delta/dR_{NH} = 0$. As a result, Δ is insensitive to changes in rate, and the region $1.4\delta > R_{NH}/2[ImH^+] > 0.7\delta$ is useless for accurate rate measurement since Δ varies by less than 10%.

Figure 1 shows representative data obtained in the pH range in which $R_{NH}/2[ImH^+] > 1.4\delta$; Figure 2 shows similar data in the pH range in which $R_{NH}/2[ImH^+] < 0.7\delta$. The data in the region of high rate (high pH) are consistent with a mixed first- and second-order rate law (eq 3). Results obtained for k_1 and k_2 are listed in

$$R_{NH} = k_1[ImH^+] + k_2[ImH^+][Im] \quad (3)$$

Table II. Because of the moderate concentrations employed, these results may be identified with $k°_1$ and $k°_2$, the rate constants at infinite dilution.

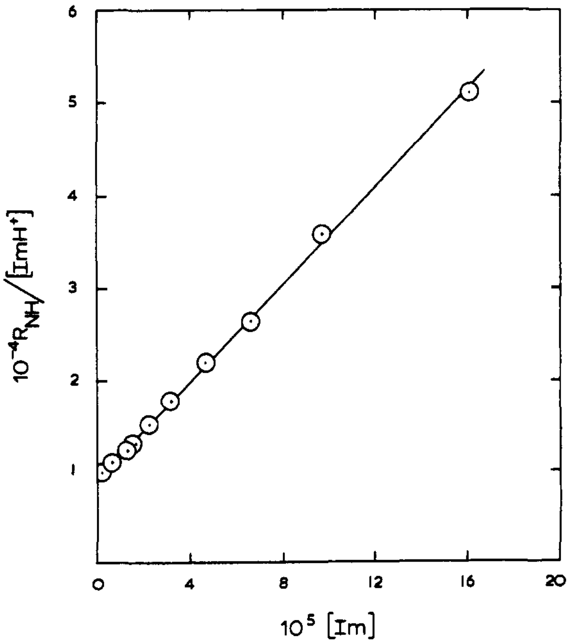


Figure 1. Plot of the specific rate of exchange of imidazolium ion *vs.* imidazole concentration in 9.98 mole % t-BuOH at 25°. The solid line is drawn according to the rate law, eq 3.

---

(5) E. K. Ralph and E. Grunwald, *J. Amer. Chem. Soc.*, **91**, 2422 (1969).

(6) E. K. Ralph and E. Grunwald, *ibid.*, **90**, 517 (1968).

(7) A. L. Bacarella, E. Grunwald, H. P. Marshall, and E. L. Purlee, *J. Org. Chem.*, **20**, 747 (1955).

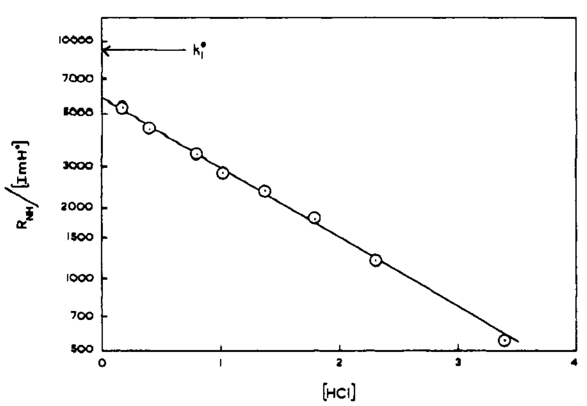


Figure 2. Plot of the specific rate of exchange for imidazolium ion *vs.* [HCl] in 9.98 mole % *t*-BuOH at 25°. The solid line is drawn according to $\log k_{cyclic} = \log k°_{cyclic} - 0.30[HCl]$.

Table II. Proton Exchange of Imidazolium Ion in *t*-BuOH–Water Mixtures Treated According to Eq 3 (pH ≈ 2–4)

t-BuOH, mole %	Temp, °C	$10^{-3}k°_1$, sec^{-1}	$10^{-8}k°_2$, $M^{-1}\,sec^{-1}$	10^7K_a
9.98	25.0	9.2	2.6_5	2.95
11.47	11.0	4.2	(1.72)[a]	1.81
11.47	21.0	6.6_5	2.07	2.68
11.47	22.25	7.8	2.01	2.80
11.47	25.0	10.0[b]	2.19	3.10
11.47	35.0	18.0	(2.52)[a]	4.42

[a] Extrapolated; $\log k°_2 = 10.492 - 642.6/T$; $E_{act} = 2.9 \pm 1.3$ kcal. [b] $\text{Log } k°_1 = 8.785 - 2326.6/T$; $E_{act} = 10.6 \pm 0.7$ kcal.

Table III. Kinetic Parameters for Proton Exchange of Imidazolium Ion in *t*-BuOH–H_2O Mixtures at 25°

	Mole % *t*-BuOH		
	0	9.98	11.47
$10^{-3}k°_1$, sec^{-1}	5.9	9.2	10.0
$10^{-3}k°_{cyclic}$, sec^{-1}	3.5	5.7	7.3
$10^{-3}k°_a$, sec^{-1}	2.4	3.5	2.7
$10^{-10}k°_{-a}$, $M^{-1}\,sec^{-1}$[a]	2.3	1.2	0.9
$10^{-8}k°_{-a}\eta$	2.0	3.8	1.2
$k°_{cyclic}/k°_a$[b]	1.5	1.6	2.7
$10^{-8}k_{2W}$, $M^{-1}\,sec^{-1}$	1.07 (0.6_2)[c]	2.5[d]	2.0
$10^{-6}k_{2W}\eta$[e]	0.95 (0.55)[c]	7.9	6.9

[a] $k°_{-a} = k°_a/K°_a$, see Table I. [b] $k°_{cyclic}//k°_a = k_H'/k_{23}$, eq 2. [c] Reference 6; figure in parentheses is for termolecular reaction in pure water. [d] Based on k_2 in Table II and k_{2A} in 11.47 mole % *t*-BuOH. [e] Units are $M^{-1}\,sec^{-1}$ poise.

Under the conditions of Figure 2, the second-order term in eq 3 is negligibly small. The gentle decrease in $R_{NH}/[ImH^+]$ with acid concentration is, therefore, an effect of HCl on k_1. As shown in Figure 2, the relationship of $\log k_1$ to [HCl] is nearly linear. However, the intercept is significantly smaller than that in Figure 2. Our interpretation of these results parallels that given to the data in water:[5] the intercept in Figure 1 is equal to $k°_a + k°_{cyclic}$; that in Figure 2 is equal to $k°_{cyclic}$. Results of this analysis are given in Table III.

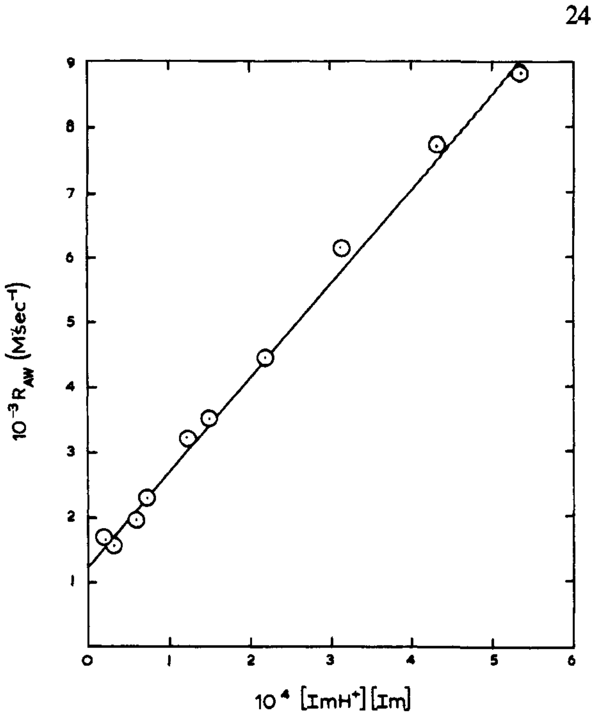


Figure 3. Plot of R_{AW} (eq 4) *vs.* $[ImH^+][Im]$ in 11.47 mole % *t*-BuOH at 25°.

Unfortunately, proton exchange resulting from acid dissociation is being repressed in the pH range in which we cannot make accurate rate measurements. A crude estimate of the parameter k_H (eq 2) is 5×10^8 sec^{-1} at 25° in 11.47 mole % *t*-BuOH.

R_{AW} and R_{WW}. The rates of proton transfer from alcohol to water (R_{AW}) and from water to water (R_{WW}) are catalyzed by imidazole buffer. Rate measurements were made at pH 6.9, where NH-OH proton exchange is too fast to give significant exchange broadening. Methods of measuring R_{AW} and R_{WW} and the catalysis of these rates by hydrogen ion have been described in the preceding paper.[8] We now report the additional catalysis, δR, by the imidazole buffer. At the given pH, δR is given precisely by the second-order rate laws

$$\delta R_{AW} = k_3[ImH^+][Im] \quad (4)$$

$$\delta R_{WW} = k_4[ImH^+][Im] \quad (5)$$

Figure 3 shows a plot of R_{AW} *vs.* $[ImH^+][Im]$ for a typical part of our data in 11.47 mole % *t*-BuOH at 25°. The slope at constant pH is equal to k_3, which is thus found to be $(1.46 \pm 0.02) \times 10^7$ $M^{-1}\,sec^{-1}$.

The data used in the evaluation of k_4 are shown in Figure 2 of the preceding paper.[8] These data are represented by the rate law, eq 4b, given in that paper, which also defines the parameter τ. On that basis, $R_{AW} + R_{WW} = (3.4 \pm 0.3) \times 10^6[ImH^+][Im]\cdot 2[H_2O]$. On introducing numerical values for $[H_2O]$ and R_{AW}, we obtain $k_4 = (2.2 \pm 0.3) \times 10^8$ $M^{-1}\,sec^{-1}$ in 11.47 mole % *t*-BuOH at 25°.

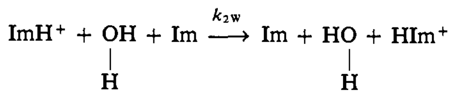
Discussion

Interpretation of Second-Order Rate Constants. We now wish to show that the values obtained for k_2, k_3, and k_4 are consistent with termolecular reaction mechanisms

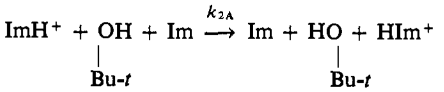
---

(8) E. Grunwald and E. K. Ralph, *J. Amer. Chem. Soc.*, **91**, 2426 (1969).

as shown in eq 6 and 7. If we proceed on that assumption,



$$\text{ImH}^+ + \underset{\text{H}}{\text{OH}} + \text{Im} \xrightarrow{k_{2W}} \text{Im} + \underset{\text{H}}{\text{HO}} + \text{HIm}^+ \qquad (6)$$



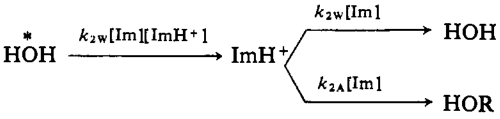
$$\text{ImH}^+ + \underset{\text{Bu-}t}{\text{OH}} + \text{Im} \xrightarrow{k_{2A}} \text{Im} + \underset{\text{Bu-}t}{\text{HO}} + \text{HIm}^+ \qquad (7)$$

then R_{NH} is given by eq 8. In interpreting k_3 and k_4, we

$$R_{NH} = (k_{2W} + k_{2A})[\text{ImH}^+][\text{Im}] \qquad (8a)$$

$$k_2 = k_{2W} + k_{2A} \qquad (8b)$$

regard the imidazole buffer as a catalyst for exchange between OH sites. The catalytic mechanism consists of two steps, as shown schematically in eq 9. The first step is reaction 6, in which the labeled proton moves from a water-OH site to an ImH$^+$ site. The second step may be either (6) or (7), and the labeled proton accordingly moves either to a new water-OH site or to a t-BuOH-OH site. The mean lifetime of the proton on the ImH$^+$ site is relatively very short. On treating ImH$^+$ as a reactive intermediate and making the steady-state approximation, we find that R_{AW} is given by eq 10a and R_{WW} by eq 11a.



$$\overset{*}{\text{H}}\text{OH} \xrightarrow{k_{2W}[\text{Im}][\text{ImH}^+]} \text{ImH}^+ \begin{cases} \xrightarrow{k_{2W}[\text{Im}]} \text{HOH} \\ \xrightarrow{k_{2A}[\text{Im}]} \text{HOR} \end{cases} \qquad (9)$$

$$R_{AW} = k_{2W}[\text{ImH}^+][\text{Im}]k_{2A}/(k_{2A} + k_{2W}) \qquad (10a)$$

$$k_3 = k_{2W}k_{2A}/(k_{2A} + k_{2W}) \qquad (10b)$$

$$R_{WW} = k_{2W}[\text{ImH}^+][\text{Im}]k_{2W}/(k_{2W} + k_{2A}) \qquad (11a)$$

$$k_4 = k_{2W}^2/(k_{2W} + k_{2A}) \qquad (11b)$$

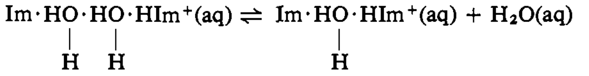
Equations 8b, 10b, and 11b express the three rate constants in terms of two parameters, k_{2W} and k_{2A}. Since the number of equations exceeds the number of parameters, the theory can be checked. Using k_2 and k_3, we find from (8b) and (10b) that $k_{2W} = (2.03 \pm 0.04) \times 10^8$ M^{-1} sec^{-1} and $k_{2A} = (1.57 \pm 0.05) \times 10^7$ M^{-1} sec^{-1}. Using k_3 and k_4, we find from (10b) and (11b) that $k_{2W} = (2.3 \pm 0.3) \times 10^8$ M^{-1} sec^{-1} and $k_{2A} = (1.56 \pm 0.02) \times 10^7$ M^{-1} sec^{-1}. The close agreement substantiates the termolecular reaction mechanism.

Rate Constants and Solvation. Fast proton-transfer reactions with solvent participation can give fairly direct information about preferential solvation in binary solvent mixtures. In the limiting case that reaction with participation by either solvent component is diffusion controlled, the relative rates for the two solvent components provide a fairly good estimate of the relative concentrations of the two reactive complexes. For example, if reactions 6 and 7 were diffusion controlled, the ratio of the rate constants, k_{2W}/k_{2A}, would be a good index of the relative concentrations of the respective termolecular encounter complexes. In the present case, $k_{2W}/k_{2A} = 12.9$ while the mole ratio of water to t-BuOH is 7.4, of the same order of magnitude. Moreover, these reactions are only slightly slower than diffusion controlled. It is therefore probable that the distribution of solvent molecules between the bulk phase and the encounter complex (Im·solvent·HIm$^+$) is nearly statistical.

Results obtained for k_{2W} at various alcohol concentrations are listed in Table III. The addition of alcohol to water is attended by two notable effects.

1. In water the reaction is partly higher than termolecular;[6] in the alchol–water mixture it is termolecular.
2. In the alcohol–water mixture k_{2W} is substantially greater than in pure water, in spite of the higher viscosity. The magnitude of the viscosity-corrected medium effect is given, approximately, by ηk_{2W}, where η is the bulk viscosity, since there is precedent that ηk_{2W} is constant for termolecular reactions in pure water[9] and in pure t-BuOH.[10] As shown in Table III, ηk_{2W} increases by more than a factor of 8. This large medium effect is even more striking when it is recalled that in pure water only part of the reaction is termolecular, and that the water concentration decreases with increasing alcohol content.

In the previous discussion of k_{2W} in pure water,[6] it was suggested that the formation of the termolecular complex from the quadrimolecular complex (eq 12) might be relatively slow and perhaps rate determining for termolecular reaction. It is also conceivable that the equilibrium in (12) is established rapidly, but lies on the left in water. In either case we would infer from the higher value of k_{2W} that the analog of the desolvation step (12) is more facile in the t-BuOH–water mixtures. A possible and plausible interpretation is that water molecules in the bulk solvent are stabilized in the presence of t-BuOH.



$$\text{Im}\cdot\underset{\text{H}}{\text{HO}}\cdot\underset{\text{H}}{\text{HO}}\cdot\text{HIm}^+(\text{aq}) \rightleftharpoons \text{Im}\cdot\underset{\text{H}}{\text{HO}}\cdot\text{HIm}^+(\text{aq}) + \text{H}_2\text{O}(\text{aq}) \qquad (12)$$

In contrast to k_{2W}, the rate constant k_{-a} for reaction of hydrogen ion with imidazole decreases monotonically as t-BuOH is added. Moreover, ηk_{-a} is far less variable than ηk_{2W}, as shown in Table III. The reaction appears to be diffusion controlled and does not show the characteristic solvent effects noted for reaction 6.

Table III also lists values of the ratio $k^\circ_{\text{cyclic}}/k^\circ_{\text{a}}$. According to the mechanism shown in eq 2, this ratio is equal to k_H'/k_{23} for reaction of the ionized intermediate.[5] Since k_H' and k_{23} both involve the breaking of a hydrogen bond, one might expect their ratio to be quite insensitive to solvent composition. This is in agreement with observation.

Experimental Section

The purification of materials, pH measurements, measurement of nuclear magnetic relaxation times of the solvent-OH protons, and the parameters used in evaluating t-BuOH–H$_2$O exchange have all been described previously.[5,8]

The parameters needed for converting experimental exchange broadenings to rates of NH-solvent exchange were obtained as follows. The ^{14}N–H coupling constant was taken to be the same as that in water.[5] The T^1 relaxation time of ^{14}N in the mixed solvents was calculated from the value in water at 25° (5.7 msec) by assuming that, in the mixed solvent, T^1 is proportional to T_1 of the solvent-OH protons.[8] The chemical shift between NH and solvent-OH protons was obtained at 56.4 MHz from the maximum exchange broadening,[5] and was 10.2 ppm (3630 ± 60 sec^{-1}) in 9.98 mole % t-BuOH and 9.3 ppm (3300 ± 150 sec^{-1}) in 11.47 mole % t-BuOH at 25°. The effect of temperature on δ was less than the experimental error in 11.47 mole % t-BuOH between 11 and 35°.

---

(9) E. Grunwald, P. J. Karabatsos, R. A. Kromhout, and E. L. Purlee, *J. Chem. Phys.*, **33**, 556 (1960).

(10) M. Cocivera, *J. Amer. Chem. Soc.*, **88**, 677 (1966).